

IN THE CLAIMS

Please amend the claims as follows:

1 (original): A method for distinguishing MLL-PTD-positive AML from other AML subtypes in a sample, the method comprising determining the expression level of markers selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, 2, and/or 3,

wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1

is indicative for the presence of PTD (MLL-PTD-positive AML with normal karyotype) when PTD is distinguished from AML_NK (MLL-PTD-negative AML with normal karyotype),

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 15, 16, 18, 19, 20, 21, 22, 23, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 42, 44, 45, 47, 48, 49, and/or 50 of Table 2.1, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 10, 13, 17, 24, 25, 41, 43, and/or 46, of Table 2.1,

is indicative for M4eo when M4eo is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20, 21, 22, 23, 24, 25, 26, 28, 29, 31, 32, 33, 34, 35, 36, 38, 39, 41, 42, 44, 45, 46, 48, 49, and/or 50 of Table 2.2, and/or

a higher expression of 5, 13, 18, 27, 30, 37, 40, 43, and/or 47, of Table 2.2

is indicative for PTD when PTD is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 49, and/or 50 of Table 2.3, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 34, and/or 48, of Table 2.3

is indicative for inv3 when inv3 is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 5, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, and/or 50 of Table 2.4, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 4, 6, 7, 8, 22, 24, 40, and/or 49, of Table 2.4

is indicative for t(15;17) when t(15;17) is distinguished from all other subtypes, and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.5

is indicative for t(8;21) when t(8;21) is distinguished from all other subtypes, and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 45, 46, 47, 48, 49, and/or 50 of Table 2.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 12, 15, 29, 41, and/or 44, of Table 2.6

is indicative for tMLL when tMLL is distinguished from all other subtypes, and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 7, 10, 12, 13, 16, 17, 19, 23, 25, 30, 31, 32, 33, 34, 37, 41, 43, 45, 47, 48, and/or 50 of Table 3.1, and/or

a higher expression a polynucleotide defined by any of the numbers 3, 6, 8, 9, 11, 14, 15, 18, 20, 21, 22, 24, 26, 27, 28, 29, 35, 36, 38, 39, 40, 42, 44, 46, and/or 49, of Table 3.1,

is indicative for M4eo when M4eo is distinguished from PTD, and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 5, 6, 9, 12, 23, 28, 38, 41, 44, 45, 46, and/or 47, of Table 3.2, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 7, 8, 10, 11, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 24, 25, 26, 27, 29, 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 42, 43, 48, 49, and/or 50 of Table 3.2,

is indicative for M4eo when M4eo is distinguished from inv3,

a lower expression of at least one polynucleotide defined by any of the numbers 2, 3, 4, 6, 11, 14, 20, 22, 26, 31, 32, 33, 34, 39, 40, 41, and/or 48, of Table 3.3, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 5, 7, 8, 9, 10, 12, 13, 15, 16, 17, 18, 19, 21, 23, 24, 25, 27, 28, 29, 30, 35, 36, 37, 38, 42, 43, 44, 45, 46, 47, 49, and/or 50 of Table 3.3,

is indicative for M4eo when M4eo is distinguished from t(15;17),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 7, 31,
40, and/or 49, of Table 3.4, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2,
3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 32,
33, 34, 35, 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, and/or 50 of Table 3.4

is indicative for M4eo when M4eo is distinguished from t(8;21),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3,
10, 14, 17, 18, 19, 21, 24, 25, 26, 31, 32, 34, 41, 44, and/or 50 of Table 3.5, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 4,
5, 6, 7, 8, 9, 11, 12, 13, 15, 16, 20, 22, 23, 27, 28, 29, 30, 33, 35, 36, 37, 38, 39, 40, 42, 43, 45, 46,
47, 48, and/or 49, of Table 3.5

is indicative for M4eo when M4eo is distinguished from tMLL,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 4, 6, 9,
28, 30, 32, 35, 37, 44, 45, and/or 48, of Table 3.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2,
3, 5, 7, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 29, 31, 33, 34, 36,
38, 39, 40, 41, 42, 43, 46, 47, 49, and/or 50 of Table 3.6

is indicative for PTD when PTD is distinguished from inv3,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3,
4, 6, 7, 10, 11, 12, 13, 14, 15, 16, 17, 18, 20, 23, 27, 28, 29, 30, 31, 32, 33, 34, 36, 38, 39, 41, 43,
44, 45, 47, 48, and/or 50 of Table 3.7, and/or

a higher expression of polynucleotide defined by any of the numbers 5, 8, 9, 19, 21, 22,
24, 25, 26, 35, 37, 40, 42, 46, and/or 49, of Table 3.7,

is for PTD when PTD is distinguished from t(15;17),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 7, 9,
10, 11, 13, 16, 20, 21, 22, 23, 30, 35, 36, 38, 42, 45, and/or 50 of Table 3.8, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2,
3, 4, 5, 6, 8, 12, 14, 15, 17, 18, 19, 24, 25, 26, 27, 28, 29, 31, 32, 33, 34, 37, 39, 40, 41, 43, 44, 46,
47, 48, and/or 49, of Table 3.8

is indicative for PTD when PTD is distinguished from t(8;21),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 5, 8, 10, 11, 13, 15, 17, 19, 25, 26, 28, 29, 34, and/or 46, of Table 3.9, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 3, 4, 6, 7, 9, 12, 14, 16, 18, 20, 21, 22, 23, 24, 27, 30, 31, 32, 33, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 47, 48, 49, and/or 50 of Table 3.9

is indicative for PTD when PTD is distinguished from tMLL,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 28, 29, 32, 33, 36, 38, 39, 40, 43, 44, 45, 46, 47, and/or 49, of Table 3.10, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 22, 27, 30, 31, 34, 35, 37, 41, 42, 48, and/or 50 of Table 3.10,

is indicative for inv(3) when inv(3) is distinguished from t(15;17),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 5, 6, 9, 11, 12, 15, 17, 18, 19, 23, 27, 35, 36, 37, 39, 42, 43, 47, 49, and/or 50 of Table 3.11, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 3, 4, 7, 8, 10, 13, 14, 16, 20, 21, 22, 24, 25, 26, 28, 29, 30, 31, 32, 33, 34, 38, 40, 41, 44, 45, 46, and/or 48, of Table 3.11

is indicative for inv(3) when inv(3) is distinguished from t(8;21),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 4, 6, 7, 8, 12, 14, 15, 16, 17, 18, 19, 20, 21, 23, 25, 26, 28, 29, 30, 31, 33, 34, 35, 37, 38, 39, 42, 43, 44, 45, 47, 48, and/or 50 of Table 3.12, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 5, 9, 10, 11, 13, 22, 24, 27, 32, 36, 40, 41, 46, and/or 49, of Table 3.12

is indicative for inv(3) when inv(3) is distinguished from tMLL,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 3, 4, 7, 14, 16, 20, 22, 23, 24, 25, 26, 30, 35, 36, 37, 39, 40, 43, 44, 46, and/or 50 of Table 3.13, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 5, 6, 8, 9, 10, 11, 12, 13, 15, 17, 18, 19, 21, 27, 28, 29, 31, 32, 33, 34, 38, 41, 42, 45, 47, 48, and/or 49 of Table 3.13,

is indicative for t(15;17) when t(15;17) is distinguished from t(8;21),
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 13, 15, 25, 26, 27, 28, 30, 32, 33, 35, 36, 38, 39, 43, 48, and/or 49, of Table 3.14, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 29, 31, 34, 37, 40, 41, 42, 44, 45, 46, 47, and/or 50 of Table 3.14,

is indicative for t(15;17) when t(15;17) is distinguished from tMLL,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 15, 16, 18, 19, 21, 23, 24, 25, 26, 27, 28, 29, 30, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 43, 44, 47, 48, of Table 3.15, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 12, 14, 17, 20, 22, 31, 37, 45, 46, 49, and/or 50 of Table 3.15,

is indicative for t(8;21) when t(8;21) is distinguished from tMLL.

2 (original): The method according to claim 1 wherein the polynucleotide is labelled.

3 (currently amended): The method according to claim 1 ~~or 2~~, wherein the label is a luminescent, preferably a fluorescent label, an enzymatic or a radioactive label.

4 (currently amended): The method according ~~at least one of the claims 1-3 to~~ claim 1, wherein the expression level of at least two, preferably of at least ten, more preferably of at least 25, most preferably of 50 of the markers of at least one of the Table 1.1-3.15 is determined.

5 (currently amended): The method according to ~~at least one of the claims 1-4~~ claim 1, wherein the expression level of markers expressed lower in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold lower, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold lower in the first subtype.

6 (currently amended): The method according to ~~at least one of the claims 1-4~~ claim 1, wherein the expression level of markers expressed higher in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold higher, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold higher in the first subtype.

7 (currently amended): The method according to ~~at least one of the claims 1-6~~
claim 1, wherein the sample is from an individual having AML.

8 (currently amended): The method according to ~~at least one of the claims 1-7~~
claim 1, wherein at least one polynucleotide is in the form of a transcribed polynucleotide, or
a portion thereof.

9 (original): The method according to claim 8, wherein the transcribed
polynucleotide is a mRNA or a cDNA.

10 (original): The method according to claim 8 ~~or 9~~, wherein the determining of
the expression level comprises hybridizing the transcribed polynucleotide to a complementary
polynucleotide, or a portion thereof, under stringent hybridization conditions.

11 (currently amended): The method according to ~~at least one of the claims 1-7~~
claim 1, wherein at least one polynucleotide is in the form of a polypeptide, or a portion
thereof.

12 (currently amended): The method according to claim 8, ~~9 or 12~~, wherein the
determining of the expression level comprises contacting the polynucleotide or the
polypeptide with a compound specifically binding to the polynucleotide or the polypeptide.

13 (original): The method according to claim 12, wherein the compound is an
antibody, or a fragment thereof.

14 (currently amended): The method according to ~~at least one of the claims 1-13~~
claim 1, wherein the method is carried out on an array.

15 (currently amended): The method according to ~~at least one of the claims 1-14~~
claim 1, wherein the method is carried out in a robotics system.

16 (currently amended): The method according to ~~at least one of the claims 1-15~~
claim 1, wherein the method is carried out using microfluidics.

17 (currently amended): Use of at least one marker as defined in ~~at least one of the claims 1-3~~ claim 1, for the manufacturing of a diagnostic for distinguishing MLL-PTD-positive AML from other AML subtypes.

18 (original): The use according to claim 17 for distinguishing MLL-PTD-positive AML from other AML subtypes in an individual having AML.

19 (currently amended): A diagnostic kit containing at least one marker as defined in ~~at least one of the claims 1-3~~ claim 1, for distinguishing MLL-PTD-positive AML from other AML subtypes, in combination with suitable auxiliaries.

20 (original): The diagnostic kit according to claim 19, wherein the kit contains a reference for the MLL-PTD-positive AML subtypes.

21 (original): The diagnostic kit according to claim 20, wherein the reference is a sample or a data bank.

22 (original): An apparatus for distinguishing MLL-PTD-positive AML from other AML subtypes in a sample containing a reference data bank.

23 (original): The apparatus according to claim 22, wherein the reference data bank is obtainable by comprising

(a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, 2, 3, 4, 5, 6 and/or 7, and

(b) classifying the gene expression profile by means of a machine learning algorithm.

24 (original): The apparatus according to claim 23, wherein the machine learning algorithm is selected from the group consisting of Weighted Voting, K-Nearest Neighbors, Decision Tree Induction, Support Vector Machines, and Feed-Forward Neural Networks, preferably Support Vector Machines.

25 (currently amended): The apparatus according to ~~at least one of the claims 22-24~~ claim 22, wherein the apparatus contains a control panel and/or a monitor.

26 (original): A reference data bank for distinguishing MLL-PTD-positive AML from other AML subtypes obtainable by comprising

- (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, 2, 3, 4, 5, 6 and/or 7, and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

27 (original): The reference data bank according to claim 26, wherein the reference data bank is backed up and/or contained in a computational memory chip.